

Amendment and Response [Under 37 C.F.R. §1.116 - Expedited Examining Procedure]

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Applicant(s): Boldogh et al.

Serial No.: 10/691,157

Confirmation No.: 6536

Filed: 22 October 2003

For: USE OF COLOSTRININ, CONSTITUENT PEPTIDES THEREOF, AND ANALOGS THEREOF AS MODULATORS OF INTRACELLULAR SIGNALING MOLECULES

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Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

Listing of Claims

1. (Currently Amended) A method of modulating an intracellular signaling molecule in a cell, the method comprising contacting the cell with an effective amount of a modulator selected from the group consisting of colostrinin, a constituent peptide of colostrinin, ~~an active analog of a constituent peptide of colostrinin~~, and combinations thereof, under conditions effective to accomplish at least one of the following:

reduce 4-hydroxynonenal (4HNE)-protein adduct formation;

inhibit 4HNE-mediated glutathione depletion;

inhibit 4HNE-induced activation of p53 protein; or

inhibit 4HNE-induced activation of c-Jun NH2-terminal kinases;

wherein the constituent peptide of colostrinin is selected from the group consisting of MQPPPLP (SEQ ID NO:1) LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLPFFQVQS (SEQ ID NO:3), LFFFLPVNVLP (SEQ ID NO:4), DLEMPVLPVEFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and ~~LKFPFKLVFVFPF~~ LKPFPLKVEVFPPF (SEQ ID NO:8);

~~wherein the active analog of a constituent peptide of colostrinin comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to a constituent peptide of colostrinin selected from the group consisting of MQPPPLP (SEQ ID NO:1) LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLPFFQVQS (SEQ ID NO:3), LFFFLPVGVLP (SEQ ID NO:4), DLEMPVLPVEFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKFPFKLVFVFPF (SEQ ID NO:8); and~~

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~~further wherein the active analog accomplishes at least one of the following: reduces 4HNE-  
protein adduct formation; inhibits 4HNE-mediated glutathione depletion; inhibits 4HNE-induced  
activation of p53 protein; or inhibits 4HNE-induced activation of c-Jun NH2-terminal kinases.~~

2. (Original) The method of claim 1 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.

3. (Original) The method of claim 1 wherein the cell is a mammalian cell.

4. (Original) The method of claim 3 wherein the cell is a human cell.

5. (Original) The method of claim 1 wherein the modulator is a constituent peptide of colostrinin.

6. (Previously Presented) The method of claim 5 wherein the modulator is selected from the group of MQPPPLP (SEQ ID NO:1), LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLPQFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPPV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPPFKLKVEVFPFP (SEQ ID NO:8), and combinations thereof.

7. (Currently Amended) A method of down regulating the 4-hydroxynonenal (4HNE)-mediated oxidative damage associated with lipid peroxidation in a cell, the method comprising contacting the cell with an effective amount of a modulator selected from the group consisting of colostrinin, a constituent peptide of colostrinin, ~~an active analog of a constituent peptide of colostrinin;~~ and combinations thereof;

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wherein the constituent peptide of colostrinin is selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:8;

~~wherein the active analog of a constituent peptide of colostrinin comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to a one or more constituent peptide of colostrinin selected from the group consisting of MQPPPLP (SEQ ID NO:1) LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLPFQVQS (SEQ ID NO:3), LFTFLPVGVLP (SEQ ID NO:4), DLEMPVLPVEPFFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPTPEKVEVTFPP (SEQ ID NO:8); and further wherein the active analog does not interfere with cellular uptake of redox-sensitive 2',7'-dihydro-dichlorofluorescein diacetate;~~

and wherein 4HNE-mediated oxidative damage associated with lipid peroxidation in the cell is down regulated.

8-9. (Cancel)